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09/636,491	08/11/2000	Josef Neu	UF-242X	9263

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EXAMINER	
MOHAMED, ABDEL A	
ART UNIT	PAPER NUMBER
1653	7

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No. 09/636,491	Applicant(s) NEU, JOSEF	
	Examiner Abdel A. Mohamed	Art Unit 1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *7-12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 13-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-18* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4,5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

ACKNOWLEDGMENT OF IDS AND STATUS OF THE CLAIMS

1. The information disclosure statement (IDS) and Form PTO-1449 filed 11/20/00, 3/1/02 and 5/15/02, respectively are acknowledged, entered and considered. Claims 1-18 are present for examination.

ELECTION/RESTRICTIONS

2. Claims 1-6, drawn to a peptide composition comprising an arginy-glutamine dipeptide formulated as a nutrient formulation will be examined along with any elected groups.

3. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-6 and 7-12, drawn to a method for promoting healthy muscle tissue by administering a dipeptide composition comprising an arginyl-glutamine formulated as a nutrient formulation classified in class 424, subclass 177.

II. Claims 1-7 and 13-18, drawn to a method for promoting increased immunity to pathogens by administering an arginyl-glutamine dipeptide formulated as a nutrient formulation, classified in class 514, subclass 19.

4. The inventions are distinct, each from the other because:

Although Inventions I-II are related because they use the same dipeptide compound/composition; however, methods for the aforementioned promotion entities are divergent and a search conducted for one would not necessarily overlap with a search conducted for another. Further, inventions I-II differ in method of promoting steps (i.e., method of promoting healthy muscle tissue versus method of promoting increased immunity to pathogens), parameters and purposes used, and as such, one does not require the other for ultimate use and is capable of separate manufacture, use and sale, and is novel and patentable over each other.

5. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification and because the searches for individual subject groups are not coextensive, restriction for examination purposes as indicated is proper.

6. During a telephone conversation with David R. Saliwanchik on 9/10/02 a provisional election was made without traverse to prosecute the invention of Group II, claims 1-6 and 13-18. Affirmation of this election must be made by applicant in replying to this Office action. Claims 7-12 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Thus, the Office action is directed to the merits of claims 1-6 and 13-18 as *per* elected invention.

7. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

CLAIMS REJECTION-35 U.S.C. § 112[2nd] PARAGRAPH

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 and 13-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 recites the limitation "the concentration" in line 1. There is insufficient antecedent basis for this limitation in claim 1 or claim 4.

Claim 4 is indefinite in the recitation "from about....to about.....". The phrase "from about....to about...." makes the claim indefinite because it is unclear as to the definite ranges since the cited phrase encompasses variations of ranges/limitations. Thus, amendment of the claim to recite "about....to about..." (i.e., deletion of "from") would obviate this rejection.

Claim 13 is indefinite and confusing in the recitation "in need of such treatment" because it is not clear to which treatment the claim is referring since the preamble of the claim is directed to a method for promoting increased immunity to pathogens.... Appropriate clarification is required.

CLAIMS REJECTION-35 U.S.C. § 112 FIRST PARAGRAPH

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-6 and 13-18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instantly claimed invention is directed to a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation, wherein said formulation is suitable for enteral or parenteral administration and further comprises an additive selected from the group consisting of vitamins, minerals, trace elements, fats, monosaccharides and oligosaccharides, wherein said monosaccharide is glucose (claims 1-6). The other aspect of the instantly claimed invention is directed to the use the above dipeptide composition in a method for promoting increased immunity to pathogens in an animal or a human, wherein said pathogen is selected from the group consisting of bacteria, viruses and parasites, and wherein said immunity is mucosal immunity comprising an IgA response to said pathogen (claims 13-18). Applicant's teachings do not adequately explain the evidence of using a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation for promoting increased immunity to pathogens in a human or an animal, wherein said human or animal is an employee,

worker or patient in a hospital or medical facility as claimed in claims 1-6 and 13-18 in the instant invention.

In this regard, the application disclosure and claims have been compared *per* the factors indicated in the decision *In re Wands*, 8 USPQ2 1400 (Fed. Cir., 1988) as to enablement and undue experimentation. The factors include:

1) the nature of the invention;

2) the breadth of the claims;

3) the predictability or unpredictability of the art;

4) the amount of direction or guidance presented;

5) the presence or absence of working examples;

6) the quantity of experimentation necessary;

7) the state of the prior art; and

8) the relative skill of those skilled in the art;

Each factor is addressed below on the basis of comparison of the disclosure, the claims and state of the prior art in the assessment of enablement (i.e., to make and/or use the invention).

1) the nature of the invention;

The instantly claimed invention is directed to a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation, wherein said formulation is administered in a method for promoting increased immunity to pathogens (i.e., effective immune responses) in an animal or a human.

2) the breadth of the claims;

The scope of the claims include a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation and a method for promoting increased immunity to pathogens in a human or animal by administering said formulation thereof. The specification does not disclose one reasonable method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claims because Applicant's teachings do not adequately explain the evidence of using the peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation for promoting increased immunity enablement to all kinds of pathogens (i.e., all kinds of bacteria, viruses and parasites) in a human or animal (any kind of animal) in the manner claimed in claims 1-6 and 13-18 in the instant invention.

Further, the first paragraph of 35 U.S.C. 112 requires, *inter alia,*that a patent specification provides sufficient guidance to enable a person skilled in the art to make and use the claimed invention without undue experimentation. *In re Vaeck,*947 F.2d 488, 495, 20 USPQ2d 1438, 1444 (Fed. Cir. 1991). While patent Applicants are not directed to disclose every species that falls within a generic claim, *id.* At 496, 20 USPQ2d at 1445, it is well settled that "the scope of the claims must bear a reasonable correlation to the scope of the enablement provided by the specification". *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

3) the predictability or unpredictability of the art;

As admittedly acknowledged on page 2, lines 23-29 in the instant specification and as taught by Madsen et al. (U.S. Patent No. 5,189,016), experiments involving the use of total parenteral nutrition (TPN) containing glycyl-glutamine dipeptide (Commercial name Dipeptiven) and alanyl-glutamine dipeptide (Commercial name Glamin), suggest potential adverse effects of the TPN formulation containing the above commercially available dipeptide. The instant specification states to this date, there are no studies of the claimed arginyl-L-glutamine dipeptide. Further, on page 3, lines 6-8, the instant specification acknowledges by stating that there remains a great need in the art for compositions and methods which promote healthy muscle tissue, reduce muscle deterioration and/or promote a healthy immune system. However, on page 4, lines 22-26, the instant specification states that among the advantages of the dipeptide of the subject invention (i.e., arginyl-glutamine) over the existing commercially available alanyl-glutamine and glycyl-glutamine dipeptide is that the arginine moiety is particularly advantageous because it is a creatine phosphate precursor, a stimulator of immune function, a stimulator of growth hormone production and, in combination with glutamine, is particularly useful in strengthening mucosal immune defenses. Nevertheless, there is no data or evidence in the instant specification to substantiate the above statement.

Furthermore, the reference of Neu et al., The FASEB Journal, Vol. 10, pp. 829-837, June 1996 (i.e., Neu is the inventor of the instantly claimed invention), the reference under the title "Glutamine nutrition and metabolism: Where do we go from here?" reviews concepts of

glutamine biochemistry, metabolism, and nutrition. On page 834, left column, the reference states that the mechanisms for these beneficial effects (i.e., glutamine biosynthesis activity) remain poorly understood, but these studies offer a stimulus for further investigation. On the same page, right column, the reference concludes by stating this is an interesting area for future studies designed to explore the mechanism of benefits derived from glutamine supplementation. An improved understanding of these mechanisms could be applied to several other critical disease processes where glutamine supplementation or metabolism may play a role. Thus, clearly suggesting for further investigation of glutamine as a potentially useful as nutritional supplementation in promoting effective immune response.

Moreover, Moinard et al. (Journal of Leukocyte Biology, Vol. 67, pp. 834-840, June 2000) discloses the involvement of glutamine, arginine, and polyamines in the action of ornithine α-ketoglutarate (OKG) on macrophage functions in stressed rats, wherein an oral administration of an equimolar amount of glutamine failed to reproduce the OKG-mediated effect. The result demonstrated by underlining the complexity of the mechanism of action of OKG, which can differ according to the functions of even a single cell type. Similarly, the reference of Robinson et al. (Clinical Science, Vol. 97, No. 6, pp. 657-669, 1999) describes the comparisons of glutamine, arginine, and OKG. In theory, these nutrients are metabolically interconvertable by known pathways, each potentially being a biosynthetic precursor of the others. Since, it is not clear which of Arg, Gln and OKG is most critical to anti-tumor defense, and since they have not been compared systematically with one another in an internally controlled study, their relative

efficacy is difficult to estimate (See e.g, page 658, left column, last paragraph). On page 667, under "Diet and immune function" the reference states that unfortunately, the design of most studies has been such that it is not possible to draw conclusions as to the efficacy of individual nutrients for improving immunity. Thus, clearly showing the unpredictable nature of compounds in the method of promoting effective immune responses to all kinds of pathogens in a human or animal in the manner claimed.

4) the amount of direction or guidance presented;

The specification discloses protocols and incorporates references improperly as recited on pages 1-6 in the instant disclosure for a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation and a method for promoting increased immunity to pathogens in a human or animal by administering said formulation thereof. However, there is no evidence or data to show that a similar regimen can be used for promoting increased immunity to pathogens using the dipeptide thereof in the manner claimed.

5) the presence or absence of working examples;

The instant specification does not enable for a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation, wherein said formulation is suitable for enteral or parenteral administration and further comprises an additive selected from the group consisting of vitamins, minerals, trace elements, fats, monosaccharides and oligosaccharides, wherein said monosaccharide is glucose (claims 1-6). The other aspect of the instantly claimed invention is directed to the use the above dipeptide composition in a method for

promoting increased immunity to pathogens in an animal or a human, wherein said pathogen is selected from the group consisting of bacteria, viruses and parasites, and wherein said immunity is mucosal immunity comprising an IgA response to said pathogen (claims 13-18). Thus, Applicant's teachings do not adequately explain the evidence of making and using claimed dipeptide for a method of promoting increased immunity to all kinds of pathogens because there are no working examples or data in the instant specification substantiating the above making and using the above dipeptide for the method claimed in the instant invention; except for protocols.

6) the quantity of experimentation necessary;

In view of the broad diversity of pathogens which encompass any kind of bacteria, virus and parasite of animals and humans, in view of the fact that animals and humans are out bread, in view of the fact that the related dipeptide have potentially adverse effects as acknowledged on page 2, lines 23-29 in the instant specification, in view of the fact that the instant specification lacks working example(s), and in view of the recognized problems and particular need in the art for using dipeptide compositions for methods which promote healthy muscle tissue, reduce muscle deterioration and/or promote a healthy immune; a reasonable doubt exists as to the enablement of the claimed method for promoting increased immune responses in all kinds of pathogens, particularly all types of bacteria, virus and parasite in all kinds of animals including humans. The claims are based on pure speculation that the methods would be effective. Therefore, undue experimentation is necessary to determine if and under what conditions, the claimed invention as broadly claimed is enabled, since promotion of effective immune responses

to all kinds of pathogens in all kinds of animals and humans by administering presumably novel dipeptide is contemplated and is encompassed as well as a wide range of situations. The results desired appear to be highly dependent on all variables, the relationship of which are not clearly disclosed. Hence, for the reasons discussed above, Applicant has not established any *nexus* between the claimed dipeptide useful in promoting effective immune responses to any kind of pathogens in all kinds of animals including humans (i.e., there is no therapeutic evidence or data in the instant application to support such claims). Thus, Applicant should present some data or authorative references in order to fulfil 35 U.S.C. 112, first paragraph requirement. For further support, See also *In re Coilliani*, 561 F. 2d 220, 195 USPQ 150 (CCPA 1977) and *Ex parte Forman* 230 USPQ 546 (BPAI 1986). Therefore, one of skill in the art would not be able to identify a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation intended to be effective to promote increased immunity to all kinds of pathogens as encompassed in the instantly claimed invention would be effective and under what conditions.

7) the state of the prior art;

Thus, in view of the above and in view of the fact that the state of the prior art as admittedly acknowledged by Applicant on page 2, lines 23-29 that experimentally involving use of TPN containing glycyl-glutamine dipeptide (related dipeptide to the instantly claimed dipeptide) suggest potential adverse effects and to this date, there are no studies of the claimed dipeptide arginyl-glutamine. Hence, one of skill in the art would not accept the characterization

of any and all effective immune responses to all kinds of pathogens by administration of the dipeptide claimed protocols without working example(s) or data or evidence as believable on their face.

8) the relative skill of those skilled in the art;

Therefore, applying the Wands factors to the facts of this case, one of skill in the art would find that undue amount of experimentation would be required to practice the full scope of the extremely broad claims for the reasons given above. Thus, in view of the quantity of experimentation necessary, the lack of adequate guidance or working examples or data, and the breadth of the claims; the claims are not commensurate in scope with the enabling disclosure. Hence, in consideration of each of factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teachings, and guidance presented. Therefore, Applicant has not disclosed to one of ordinary skill in the art how to use a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation for promoting increased immunity to all kinds of pathogens in animals including humans. There is insufficient written description of the invention with respect to the *in vivo* enablement of the methods to enable one of ordinary skill in the art to use Applicant's invention for the reasons discussed above. Accordingly, the requirement of 35 U.S.C. 112, first paragraph of "how to use" has not been met. Therefore, it is viewed that the specification does not enable the invention as claimed in claims 1-6 and 13-18, as it does not teach how to use the invention to achieve the function of the claims.

CLAIMS REJECTION-35 U.S.C. § 102(b)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Miyazawa et al. (Journal of the Faculty of Fisheries and Animal Husbandry Hiroshima, Vol. 15 No. 2, pp. 161-169, 1976, Abstract only from Database Biosis Online).

The abstract of Miyazawa et al. discloses a peptide composition comprising an arginyl-glutamine dipeptide formulation in large quantities from 7 species of marine green algal extracts.

The abstract does not disclose the intended use of the nutrient formulation comprising an arginyl-glutamine dipeptide (claim 1), the formulation is suitable for enteral administration (claim 2), and the formulation is suitable for parenteral administration (claim 3), respectively. Nevertheless, a statement of usefulness or contemplated use of a claimed compound or composition in a claim is usually given little weight in distinguishing over the prior art. *In re Maeder et al.* (CCPA 1964) 337 F2d 875, 143 USPQ 248; *In re Riden et al.* (CCPA 1963) 318 F2d 761, 138 USPQ 112; *In re Sinex* (CCPA 1962) 309 F2d 488, 135 USPQ 302. Further, it is well established that the intended use of a compound (e.g., a polypeptide or a protein or a glycoprotein) does not impart patentability to the compound. *In re spada,* 911 F.2d 70, 15

USPQ2d 1655 (Fed. Cir. 1990) (The discovery of a new property or use of a previously known composition, even when that property and use are unobvious from the prior art, can not impart patentability to claims to the known composition); *In re Pearson*, 494 F.2d 1399, 1403, 181 USPQ 641, 644 (CCPA 1974) (intended use of an old composition does not render composition claims patentable); *In re Zierden*, 411 F.2d 1325, 1328, 162 USPQ 102, 104 (CCPA 1969). Thus, in the absence of evidence to the contrary or specific structural limitations, the claimed composition/product disclosed by the reference anticipates claims 1-3 as drafted.

11. Claims 1-6 are rejected under 35 U.S.C. 102(b) as being anticipated by JP2119762.

JP2119762 discloses a nutrient composition formulated with an essential amino acid and at least one oligopeptide selected from the group consisting of a dipeptide wherein the dipeptide is arginyl-glutamine (See e.g., page 7, line 12), wherein said formulation is suitable for enteral administration (See e.g., page 8, line 6), wherein said formulation is suitable for parenteral administration (See e.g. page 11, last two lines), and wherein said nutrient formulation comprises additives such as glucose, electrolyte, vitamins and trace elements (See e.g. ,page 15, paragraph 2). Thus, the reference clearly discloses a peptide composition comprising an arginyl-glutamine dipeptide formulated as nutrient formulation in the manner claimed in claims 1-3 and 5-6.

With respect to the concentration of claim 4, the concentration is not disclosed in the prior art in the manner claimed; however, the claim as drafted recites a wide range of concentration of dipeptide (i.e., from about 0.1% to about 25.%) by weight of the formulation;

and does not define the concentration weight as functional limitation, rather, the claim defines the concentration weight as properties of the dipeptide formulation. Thus, it is the Examiner's position that a peptide composition comprising an arginyl-glutamine dipeptide formulated as a nutrient formulation would have the same concentration percentages by weight of said formulation as claimed, and as such, the concentration percentages is an inherent properties of the prior art dipeptide composition. Thus, in the absence of evidence to the contrary, the nutritional formulation disclosed by the reference anticipates claims 1-6 as drafted.

CLAIMS REJECTION-35 U.S.C. § 103(a)

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 and 13-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP2119762 taken with WO 98/09985 and Neu et al. (The FASEB Journal, Vol. 10, pp. 829-837, June 1966).

JP2119762 as discussed above under the rejection of 102(b) discloses a nutrient composition formulated with an essential amino acid and at least one oligopeptide selected from the group consisting of a dipeptide wherein the dipeptide is arginyl-glutamine, wherein said formulation is suitable for enteral administration, wherein said formulation is suitable for

parenteral administration, and wherein said nutrient formulation comprises additives such as glucose, electrolyte, vitamins and trace elements. The reference differs from claims 1-6 and 13-18 in not teaching a method for promoting increased immunity to pathogens in a human or an animal by administering a composition comprising an arginyl-glutamine dipeptide. However, the reference of WO 98/09985 teaches the use of anti-inflammatory peptides comprising an arginyl-glutamine dipeptide to exert an inhibitory effect on a humoral and/or cellular immune response accompanying inflammation associated with or caused by conditions such as hypersensitivity, allergic reactions, asthma, or caused by infectious diseases with viruses such as AIDS, ect., (See e.g., abstract, page 1, lines 13-21, page 4, lines 32-34, page 8, lines 4-9, page 10, lines 20-32, and Figure 3). Further, the reference of Neu et al. on page 835, column 1, third paragraph, clearly states that arginine and glutamine are both converted to citrulline and ornithine and stimulate the production of nitric oxide, which has far-reaching biological consequences on the microcirculation in both health and disease. Glutamine and arginine may improve macrophage-mediated killing of bacteria and white blood cell phagocytic function. Thus clearly suggesting that the use of arginyl-glutamine dipeptide would result in increasing the effect of immune responses to pathogens. Furthermore, the above statement would provide motivation to one of ordinary skill in the art to select these conventional dipeptide groups, particularly to use arginine in combination with glutamine with the expectation that they would work similarly to other dipeptide groups; thus rendering selection *prima facie* obvious to one of ordinary skill in the art. As pointed out in case law "The use of patents as references is not limited to what the patentees

describe as their own inventions or to the problems with which they are connected. They are part of the literature of the art, relevant for all they contain". *In re Heck*, 699 F.2d 1331, 1332-33, 216 USPQ 1038, 1039 (Fed. Cir. 1983) (quoting *In re Lemelson*, 397 F.2d 1006, 1009, 158 USPQ 275, 277 (CCPA 1968); and a reference may be relied upon for all that it would have reasonably suggested to one having ordinary skill in the art, including none preferred embodiments (emphasis provided). *Merck & Co. v. Biocraft laboratories*, 874 F.2d 804, 10 USPQ2d 1843 (Fed. Cir.), cert. denied, 493 U.S. 975 (1989). See also MPEP 2123: "Rejection Over Prior Art's Broad Disclosure Instead of Preferred Embodiments".

Therefore, given the teachings of the secondary references, one of ordinary skill in the art would be able to adapt the above scheme of applying a method for promoting increased immunity to pathogens in a human or an animal by administering the composition of the primary reference comprising an arginyl-glutamine dipeptide. Further, such features (i.e., methods of increasing effect of immune response to pathogens) are known or suggested in the art, as seen in the secondary reference, and including such features into the composition of the primary reference of JP2119762 would have been obvious to one of ordinary skill in the art to obtain the known and recognized functions and advantages thereof. Therefore, in view of the above, and in view of the combined teachings of the prior art; one of ordinary skill in the art would have been motivated at the time the invention was made to employ a peptide composition comprising a dipeptide of an arginyl-glutamine formulated as a nutrient formulation useful in a method for promoting increased immunity to pathogens in an animal or a human by administering the

dipeptide composition thereof, absent of sufficient objective factual evidence or unexpected results to the contrary.

CITATION OF RELEVANT PRIOR ART

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Mattox et al. (The Annals of Pharmacotherapy, Vol. 29, No. 2, pp. 174-180, February 1995) review that the infusion of parenteral nutrition has the potential to produce a variety of metabolic responses that could be both beneficial and harmful.

Le Boucher et al. (Nutrition, Vol. 15, No. 10, pp. 773-777, 1999) describe that glutamine and arginine derived from ornithine α-ketoglutarate (OKG) are responsible for immunomodulating properties in burn injury.

CONCLUSION AND FUTURE CORRESPONDENCE

14. Claims 1-6 and 13-18 are rejected and claims 7-12 are withdrawn from further consideration.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Abdel A. Mohamed whose telephone number is (703) 308-3966. The examiner can normally be reached on Monday through Friday from 5:30 a.m. to 5:00 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low, can be reached on (703) 308-2923. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Abdel A. Mohamed

ABDEL MOHAMED
PATENT EXAMINER
GROUP 1800
TC 1600

AAM Mohamed/AAM

December 9, 2002